EXHIBIT A

Declaration of Mandy H. Kim In Support of Halozyme, Inc.'s Motion for Partial Summary Judgment and Opposition to the U.S. Patent and Trademark Offices's Motion for Summary Judgment

IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

HALOZYME, INC., Plaintiff, v. JOSEPH MATAL, performing the functions and duties of Under Secretary of Commerce for Intellectual Property and Director of the United States Patent and Trademark Office, Defendant.	Civil Action No. 1:16-CV-01580 CMH (JFA)

DECLARATION OF MANDY H. KIM
IN SUPPORT OF HALOZYME, INC.'S MOTION FOR PARTIAL SUMMARY JUDGMENT AND OPPOSITION TO THE U.S. PATENT AND TRADEMARK OFFICE'S MOTION FOR SUMMARY JUDGMENT

I, Mandy H. Kim, declare as follows:

1. I am member of McDermott Will & Emery LLP and counsel of record for Plaintiff Halozyme, Inc. ("Halozyme") in the above-captioned matter. I have knowledge of the following, and if called as a witness, could and would testify competently to the contents herein.

2. Attached as Exhibit 1 is a true and correct copy of the July 14, 2017 Corrected Opening Expert Report of Samuel Zalipsky, Ph.D.

3. Attached as Exhibit 2 is a true and correct copy U.S. Patent Application No. 11/065,716 (the "'716 Application") (HALOZ0000001-HALOZ0000325).

4. Attached as Exhibit 3 is a true and correct copy of Sherwood *et al.*, *Enhanced plasma persistence of therapeutic enzymes by coupling to soluble dextran*, BIOCHEM. J. 164(2):461-464 (1977) (HALOZ0000326-HALOZ0000329).

5. Attached as Exhibit 4 is a true and correct copy of Orkin and Toole, *Chick*

Embryo Fibroblasts Produce Two Forms of Hyaluronidase, J. CELL BIOL. 85:248-57 (1980) (HALOZ0000330-HALOZ0000339).

6. Attached as Exhibit 5 is a true and correct copy of Beauchamp *et al.*, *A New Procedure for the synthesis of polyethylene glycol-protein adducts; effects on function, receptor recognition, and clearance of superoxide dismutase, lactoferrin, and α2-macroglobulin*, ANAL. BIOCHEM. 131:25-33 (1983) (HALOZ0000340-HALOZ0000348).

7. Attached as Exhibit 6 is a true and correct copy of Wileman *et al.*, *Potential use of an asparaginase-dextran conjugate in acute lymphoblastic leukemia*, J. PHARM. PHARMACOL. 35:762-765 (1983) (HALOZ0000349-HALOZ0000352).

8. Attached as Exhibit 7 is a true and correct copy of Berger, Jr. and Pizzo, *Preparation of polyethylene glycol-tissue plasminogen activator adducts that retain functional activity: Characteristics and behavior in three animal species*, BLOOD 71(6):1641-1647 (1988) (HALOZ0000353-HALOZ0000360).

9. Attached as Exhibit 8 is a true and correct copy of Hotchkiss *et al.*, *The influence of carbohydrate structure on the clearance of recombinant tissue-type plasminogen activator*, THROM. HAESMOT. 60(2):255-261 (1988) (HALOZ0000361-HALOZ0000368).

10. Attached as Exhibit 9 is a true and correct copy of Hadley and Sato, *Catalytic activity of administered gulonolactone oxidase polyethylene glycol conjugates*, ENZYME 42:255-234 (1989) (HALOZ0000369-HALOZ0000379).

11. Attached as Exhibit 10 is a true and correct copy of Spellman *et al.*, *Carbohydrate structures of human tissue plasminogen activator expressed in Chinese hamster ovary cells*, J. BIOL. CHEM. 264(24):14100-14111 (1989) (HALOZ0000380-HALOZ0000391).

12. Attached as Exhibit 11 is a true and correct copy of Caliceti *et al.*, *Effects of*

monomethoxypoly(ethylene glycol) modification of ribonuclease antibody recognition, substrate accessibility and conformational stability, J. MOLEC. RECOGN. 3(2):89-93 (1990) (HALOZ0000392-HALOZ0000396).

13. Attached as Exhibit 12 is a true and correct copy of Goodson and Katre, *Site-directed PEGylation of recombinant interleukin-2 at its glycosylation site*, BIOTECHNOLOGY 8:343-346 (1990) (HALOZ0000397-HALOZ0000400).

14. Attached as Exhibit 13 is a true and correct copy of Delgado *et al.*, *The uses and properties of PEG-linked proteins*, CRIT. REV. THERAPEUT. DRUG CARRIER SYS. 9(3,4):249-304 (1992) (HALOZ0000401-HALOZ0000458).

15. Attached as Exhibit 14 is a true and correct copy of Roseng *et al.*, *Uptake, intracellular transport, and degradation of Polyethylene glycol-modified asialofetuin in hepatocytes*, J. BIOL. CHEM. 267(32):22987-22993 (1992) (HALOZ0000459-HALOZ0000465).

16. Attached as Exhibit 15 is a true and correct copy of Zalipsky *et al.*, *Evaluation of new reagent for covalent attachment of polyethylene glycol to proteins*, BIOTECHNOL. APPL. BIOCHEM. 15:100-114 (1992) (HALOZ0000466-HALOZ0000481).

17. Attached as Exhibit 16 is a true and correct copy of Matsuyama *et al.*, *Changes is enzymatic and membrane-adsorbing activities of Sphingomyelinase from Bacillus cereus by modification with polyethylene glycol derivative*, CHEM. PHARM. BULL. 40(9):2478-2482 (1992) (HALOZ0000482-HALOZ0000486).

18. Attached as Exhibit 17 is a true and correct copy of Chiu *et al.*, *Enzymatic activity of chymotrypsin and its poly(ethylene glycol) conjugates toward low and high molecular weight substrates*, BIOCONJUGATE CHEM. 4:290-295 (1993) (HALOZ0000487-HALOZ0000492).

19. Attached as Exhibit 18 is a true and correct copy of Katre, *The conjugation of*

proteins with polyethylene glycol and other polymers, ADV. DRUG DEL. REV. 10:91-114 (1993) (HALOZ0000493-HALOZ0000516).

20. Attached as Exhibit 19 is a true and correct copy of Duncan and Spreafico, *Polymer Conjugates Pharmacokinetic Considerations for Design and Development*, CLIN. PHARMACOKINET. 27(4):290-306 (1994) (HALOZ0000517-HALOZ0000533).

21. Attached as Exhibit 20 is a true and correct copy of Zalipsky, *Chemistry of polyethylene glycol conjugates with biologically active molecules*, ADV. DRUG DELIV. REV. 16(2-3):157-182 (1995) (HALOZ0000534-HALOZ0000559).

22. Attached as Exhibit 21 is a true and correct copy of Dwek, Glycobiology: *Toward understanding the function of sugars*, CHEM. REV. 96:683-720 (1996) (HALOZ0000560-HALOZ0000597).

23. Attached as Exhibit 22 is a true and correct copy of Veronese *et al.*, *Branched and linear poly (ethylene glycol): Influence of the Polymer Structure on Enzymologiacal, Pharmacokinetic, and Immunological Properties of Protein Conjugates*, J. BIOACTIVE COMPATIBLE POLYM. 12:196-207 (1997) (HALOZ0000598-HALOZ0000609).

24. Attached as Exhibit 23 is a true and correct copy of Noorman *et al.*, *Inhibition of mannose receptor-mediated clearance of tissue-type plasminogen activator (t-PA) by dextran: a new explanation for its antithrombotic effect*, THROMB. HAESMOT. 78:1249-1254 (1997) (HALOZ0000610-HALOZ0000616).

25. Attached as Exhibit 24 is a true and correct copy of Knauf *et al.*, *Relationship of Effective Molecular Size to Systemic Clearance in Rats of Recombinant Interleukin-2 Chemically Modified with Water-soluble Polymers*, J. BIOL. CHEM. 263(29):15064-15070 (1988) (HALOZ0000617-HALOZ0000623).

26. Attached as Exhibit 25 is a true and correct copy of Lansink *et al.*, *Increased clearance explains lower plasma levels of tissue-type plasminogen activator by estradiol: Evidence for potently enhanced mannose-receptor expression in mice*, BLOOD 94(4):1330-1336 (1999) (HALOZ0000624-HALOZ0000631).

27. Attached as Exhibit 26 is a true and correct copy of Kamada *et al.*, *Antitumor activity of Tumor Necrosis Factor-α conjugated with polyvinylpirrolidone on solid tumors in mice*, CANCER RES. 60:6416-6420 (2000) (HALOZ0000632-HALOZ0000637).

28. Attached as Exhibit 27 is a true and correct copy of Nodake and Yamasaki, *Some Properties of a Macromolecular Conjugate of Lysozyme Prepared by Modification with a Monomethoxypolyethylene Glycol Derivative*, BIOSCI. BIOTECHNOL. BIOCHEM. 64(4):767-774 (2001) (HALOZ0000638-HALOZ0000645).

29. Attached as Exhibit 28 is a true and correct copy of Egrie and Browne, *Development and characterization of novel erythropoiesis stimulating protein (NESP)*, BRIT. J. CANCER 84(Suppl.):3-10 (2001) (HALOZ0000646-HALOZ0000653).

30. Attached as Exhibit 29 is a true and correct copy of Veronese, *Peptide and protein PEGylation: a review of problems and solutions*, BIOMATERIALS 22:405-417 (2001) (HALOZ0000654-HALOZ0000666).

31. Attached as Exhibit 30 is a true and correct copy of Kratz *et al.*, *Probing the cysteine-34 position of endogenous serum albumin with thiol-binding doxorubicin derivatives. Improved Efficacy of an acid sensitive doxorubicin derivative with specific albumin-binding properties compared to that of the parent compound*, J. MED. CHEM. 45:5523-5533 (2002) (HALOZ0000667-HALOZ0000677).

32. Attached as Exhibit 31 is a true and correct copy of Li *et al.*, *Importance of*

Glycosylation and Disulfide Bonds in Hyaluronidase Activity of Macaque Sperm Surface PH-20, J. ANDROLOGY 23(2): 211-219 (2002) (HALOZ0000678-HALOZ0000686).

33. Attached as Exhibit 32 is a true and correct copy of Mio and Stern, *Inhibitors of the hyaluronidases*, MATRIX BIOLOGY 21:31-37 (2002) (HALOZ0000687-HALOZ0000693).

34. Attached as Exhibit 33 is a copy of Kinstler *et al.*, *Mono-N-terminal poly(ethylene glycol)–protein conjugates*, ADV. DRUG DEL. REV. 54:477-485 (2002) (HALOZ0000694-HALOZ0000702).

35. Attached as Exhibit 34 is a true and correct copy of Neumann & Foote, *Megakaryocyte growth and development factor (MGDF): an Mpl ligand and cytokine that regulates thrombopoiesis*, CYTOKINES CELL MOL. THER. 6:47-56 (2000) (HALOZ0000703-HALOZ0000714).

36. Attached as Exhibit 35 is a true and correct copy of Roberts *et al.*, *Chemistry of peptide and protein PEGylation*, ADV. DRUG DEL. REV. 54:459-476 (2002) (HALOZ0000715-HALOZ0000732).

37. Attached as Exhibit 36 is a true and correct copy of Sakakibara *et al.*, *Preparation and properties of alginate lyase modified with Poly (ethylene Glycol)*, J. PHARM. SCI. 91(4):1191-1199 (2002) (HALOZ0000733-HALOZ0000741).

38. Attached as Exhibit 37 is a true and correct copy of Caliceti and Veronese, *Pharmacokinetic and biodistribution properties of poly(ethylene glycol)-protein conjugates*, ADV. DRUG DEL. REV. 55:1261–1277 (2003) (HALOZ0000742-HALOZ0000758).

39. Attached as Exhibit 38 is a true and correct copy of Harris & Chess, *Effect of Pegylation on Pharmaceuticals*, NATURE REVIEW DRUG DISCOVERY 2(3):214-221 (2003) (HALOZ0000759-HALOZ0000766).

40. Attached as Exhibit 39 is a true and correct copy of Toole, Hyaluronan: *From Extracellular Glue to Pericellular Cue*, NATURE REVIEWS 4:528-539 (2004) (HALOZ0000767-HALOZ0000778).

41. Attached as Exhibit 40 is a true and correct copy of Veronese and Pasut, *PEGylation, successful approach to drug delivery*, DRUG DISCOVERY TODAY 10(21):1451-1458 (2005) (HALOZ0000779-HALOZ0000786).

42. Attached as Exhibit 41 is a true and correct copy of Zalipsky *et al.*, *Thiolytically Cleavable Dithiobenzyl Urethane-Linked Polymer–Protein Conjugates as Macromolecular Prodrugs: Reversible PEGylation of Proteins*, BIOCONJUGATE CHEM. 18:1869-1878 (2007) (HALOZ0000787-HALOZ0000796).

43. Attached as Exhibit 42 is a true and correct copy of Fishburn, *The Pharmacology of PEGylation: Balancing PD with PK to Generate Novel Therapeutics*, J. PHARM. SCI. 97(10):4167-4183 (2008) (HALOZ0000797-HALOZ0000813).

44. Attached as Exhibit 43 is a true and correct copy of Gamblin *et al.*, *Glycoprotein Synthesis: An Update*, CHEM. REV. 109(1):131-163 (2009) (HALOZ0000814-HALOZ0000847).

45. Attached as Exhibit 44 is a true and correct copy of Roberts *et al.*, *Chemistry for peptide and protein PEGylation*, ADV. DRUG DEL. REV. 64:116-127 (2012) (HALOZ0000848-HALOZ0000859).

46. Attached as Exhibit 45 is a true and correct copy of Sherman *et al.*, *Role of the Methoxy Group in Immune Responses to mPEG-Protein Conjugates*, BIOCONJUGATE CHEM. 23:485-499 (2012) (HALOZ0000860-HALOZ0000874).

47. Attached as Exhibit 46 is a true and correct copy of Turecek *et al.*, *PEGylation of biopharmaceuticals: a review of chemistry and nonclinical safety information of approved drugs,*

J. PHARM. SCI. 105:460-475 (2016) (HALOZ0000875-HALOZ0000890).

48. Attached as Exhibit 47 is a true and correct copy of the July 14, 2017 Opening Expert Report of Bruno Flamion, Ph.D.

49. Attached as Exhibit 48 is a true and correct copy of Chain and Duthie, *Identity of hyaluronidase and spreading factor*, BR. J. EXPER. PATHOL. 21:324-338 (1940) (HALOZ0000891-HALOZ0000905).

50. Attached as Exhibit 49 is a true and correct copy of Matthews and Dorfman, *Inhibition of hyaluronidase*, PHYSIOL. REV. 35: 381 (1955) (HALOZ0000906-HALOZ0000927).

51. Attached as Exhibit 50 is a true and correct copy of Maroko *et al.*, *Reduction by hyaluronidase of myocardial necrosis following coronary artery occlusion*, CIRCULATION 46(3):430-437 (1972) (HALOZ0000928-HALOZ0000936).

52. Attached as Exhibit 51 is a true and correct copy of Maroko *et al.*, *Favorable effects of hyaluronidase on electrocardiographic evidence of necrosis in patients with acute myocardial infarction*, N. ENGL. J. MED. 296(16):898-903 (1977) (HALOZ0000937-HALOZ0000942).

53. Attached as Exhibit 52 is a true and correct copy of Salkie, *Inhibition of Wydase by human serum*, CAN. MED. ASSOC. J. 121(7):845 (1979) (HALOZ0000943-HALOZ0000944).

54. Attached as Exhibit 53 is a true and correct copy of Wolf *et al.*, T*he serum kinetics of bovine testicular hyaluronidase in dogs, rats and humans*, J. PHARMACOL. EXP. THER. 222(2):331-337 (1982) (HALOZ0000945-HALOZ0000951).

55. Attached as Exhibit 54 is a true and correct copy of Roberts *et al.*, *Effect of hyaluronidase on mortality and morbidity in patients with early peaking of plasma creatine kinase MB and non-transmural ischaemia. Multicentre investigation for the limitation of infarct*

size (MILIS), BR. HEART J. 60(4):290-298 (1988) (HALOZ0000952-HALOZ0000960).

56. Attached as Exhibit 55 is a copy of Laurent and Fraser, *Hyaluronan*, FASEB J. 6(7):2397-2404 (1992) (HALOZ0000961-HALOZ0000969).

57. Attached as Exhibit 56 is a true and correct copy of Minch *et al.*, *Tissue plasminogen activator coexpressed in Chinese hamster ovary cells with α(2,6)-sialyltransferase contains NeuAcα(2,6)Gal β(1,4)Glc-N-AcR linkages*. BIOTECHNOL. PROG. 11(3):348-351 (1995) (HALOZ0000970-HALOZ0000973).

58. Attached as Exhibit 57 is a true and correct copy of Narita *et al.*, *Two receptor systems are involved in the plasma clearance of tissue-type plasminogen activator (t-PA) in vivoI,* J. CLIN. INVEST. 96(2):1164-1168 (1995) (HALOZ0000974-HALOZ0000978).

59. Attached as Exhibit 58 is a true and correct copy of Cherr *et al.*, *The PH-20 protein in cynomolgus macaque spermatozoa: Identification of two different forms exhibiting hyaluronidase activity*, DEV. BIOL. 175:142-153 (1996) (HALOZ0000979-HALOZ0000990).

60. Attached as Exhibit 59 is a true and correct copy of Frost *et al.*, *The Hyaluronidases: A Chemical, Biological and Clinical Overview*, TRENDS IN GLYCOSCIENCE AND GLYCOTECHNOLOGY 8(44):419-434 (1996) (HALOZ0000991-HALOZ0001006).

61. Attached as Exhibit 60 is a true and correct copy of Hunnicutt *et al.*, *Sperm surface protein PH-20 is bifunctional: one activity is a hyaluronidase and a second, distinct activity is required in secondary sperm-zona binding*, BIOL. REPROD. 55:80-86 (1996) (HALOZ0001007-HALOZ0001013).

62. Attached as Exhibit 61 is a true and correct copy of Frost and Stern, *A microtiter-based assay for hyaluronidase activity not requiring specialized reagents*, ANALYTICAL BIOCHEM. 251:263-269 (1997) (HALOZ0001014-HALOZ0001020).

63. Attached as Exhibit 62 is a true and correct copy of Hascall and Laurent, Hyaluronan: *structure and physical properties*, *available at*: http://glycoforum.gr.jp/science/hyaluronan/HA01/HA01E.html (1997) (HALOZ0001021-HALOZ0001025).

64. Attached as Exhibit 63 is a true and correct copy of Meyer *et al.*, *The soluble hyaluronidase from bull testes is a fragment of the membrane-bound PH-20 enzyme*, FEBS. LETT. 413(2):385-388 HALOZ0001026-HALOZ0001029 (1997) (HALOZ0001026-HALOZ0001029).

65. Attached as Exhibit 64 is a true and correct copy of Szépfalusi *et al.*, *IgE-mediated allergic reaction to hyaluronidase in paediatric oncological patients*, URBANEK R. EUR. J. PEDIATR. 156(3):199-203 (1997) (HALOZ0001030-HALOZ0001034).

66. Attached as Exhibit 65 is a true and correct copy of Marković-Housley *et al.*, *Crystal structure of hyaluronidase, a major allergen of bee venom*, STRUCTURE 8(10):1025-35 (2000) (HALOZ0001035-HALOZ0001045).

67. Attached as Exhibit 66 is a true and correct copy of Csoka *et al.*, *The six hyaluronidase-like genes in the human and mouse genomes*, MATRIX BIOLOGY 20:499-508 (2001) (HALOZ0001046-HALOZ0001055).

68. Attached as Exhibit 67 is a true and correct copy of Mio and Stern, *Inhibitors of the hyaluronidases*, MATRIX BIOLOGY 21:31-37 (2001) (HALOZ0001056-HALOZ0001062).

69. Attached as Exhibit 68 is a true and correct copy of Oettl *et al.*, *Comparative characterization of bovine testicular hyaluronidase and a hyaluronate lyase from Streptococcus agalactiae in pharmaceutical preparations*, EUR. J. PHARM. SCI. 18(3-4):267-277 (2003) (HALOZ0001063-HALOZ0001073).

70. Attached as Exhibit 69 is a true and correct copy of Chowpongpang *et al.*, *Cloning and characterization of the bovine testicular PH-20 hyaluronidase core domain*,

BIOTECHNOL. LETT. 26(15):1247-52 (2004) (HALOZ0001074-HALOZ0001079).

71. Attached as Exhibit 70 is a true and correct copy of Mendez *et al.*, *Albumin therapy in clinical practice*, NUTR. CLIN. PRACT. 20:314-320 (2005) (HALOZ0001080-HALOZ0001086).

72. Attached as Exhibit 71 is a true and correct copy of Bookbinder *et al.*, *A recombinant human enzyme for enhanced interstitial transport of therapeutics*. J. CONTROL. RELEASE 114(2):230-241 (2006) (HALOZ0001087-HALOZ0001098).

73. Attached as Exhibit 72 is a true and correct copy of Skov *et al.*, *Structure of recombinant Ves v 2 at 2.0 Å resolution: structural analysis of an allergenic hyaluronidase from wasp venom*, ACTA CRYSTALLOGR. D. BIOL. CRYSTALLOGR. 62(Pt 6):595-604 (2006) (HALOZ0001099-HALOZ0001108).

74. Attached as Exhibit 73 is a true and correct copy of Stern and Jedrzejas, *Hyaluronidases: Their Genomics, Structures and Mechanisms of Action*, CHEM. REV. 106:818-839 (2006) (HALOZ0001109-HALOZ0001130).

75. Attached as Exhibit 74 is a true and correct copy of Taylor *et al.*, *Comparison of bovine- and recombinant human-derived hyaluronidase with regard to fertilization rates and embryo morphology in a sibling oocyte model: a prospective, blinded, randomized study*, FERTIL. STERIL. 85(5):1544-1546 (2006) (HALOZ0001131-HALOZ0001133).

76. Attached as Exhibit 75 is a true and correct copy of Chao *et al.*, *Structure of Human Hyaluronidase-1, a Hyaluronan Hydrolyzing Enzyme Involved in Tumor Growth and Angiogenesis*, BIOCHEMISTRY 46 (23):6911–6920 (2007) (HALOZ0001134-HALOZ0001143).

77. Attached as Exhibit 76 is a true and correct copy of Frost, *Recombinant human hyaluronidase (rHuPH20): an enabling platform for subcutaneous drug and fluid*

administration, EXPERT OPIN. DRUG DELIV. 4(4): 427-440 (2007) (HALOZ0001144-HALOZ0001157).

78. Attached as Exhibit 77 is a true and correct copy of Evison *et al.*, *Human recombinant hyaluronidase (Cumulase®) improves intracytoplasmic sperm injection survival and fertilization rates*, REPROD. BIOMED. ONLINE 18(6):811-814 (2009) (HALOZ0001158-HALOZ0001161).

79. Attached as Exhibit 78 is a true and correct copy of Boonen *et al.*, *Mouse liver lysosomes contain enzymatically active processed forms of Hyal-1*, BIOCHEM. BIOPHYS. RES. COMMUN. 446:1155-1160 (2014) (HALOZ0001162-HALOZ0001167).

80. Attached as Exhibit 79 is a true and correct copy of FDA label for Activase (alteplase) *available at*: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/103172s5203lbl.pdf (2015) (HALOZ0001168-HALOZ0001184).

81. Attached as Exhibit 80 is a true and correct copy of Hingorani *et al.*, *Phase 1b study of PEGylated recombinant human hyaluronidase and gemcitabine in patients with advanced pancreatic cancer*, CLIN. CANCER RES. 22(12):2848-2854 (2016) (HALOZ0001185-HALOZ0001192).

82. Attached as Exhibit 81 is a true and correct copy of Narayanan and Weekes, *Molecular therapeutics in pancreas cancer*, WORLD J. OF GASTROINTESTINAL ONCOLOGY 8(4):366-379 (2016) (HALOZ0001193-HALOZ0001207).

83. Attached as Exhibit 82 is a true and correct copy of 35th Annual J.P. Morgan Healthcare Conference, *Building a Premier Oncology Biotech: Two Pillar Strategy for Growth*, Dr. Helen Torley, President & CEO of Halozyme (2017) (HALOZ0001208-HALOZ0001234).

84. Attached as Exhibit 83 is a true and correct copy of Meshach and Rajasekaran, *In silico approach to explore the disruption in the molecular mechanism of human hyaluronidase 1 by mutant E268K that directs Natowicz syndrome*, EUR. BIOPHYS. J. 46:157–169 (2017) (HALOZ0001235-HALOZ0001247).

85. Attached as Exhibit 84 is a true and correct copy of EMA label for reteplase (Rapilysin) *available at*: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000105/WC500046734.pdf (HALOZ0001248-HALOZ0001274).

86. Attached as Exhibit 85 is a true and correct copy of EMA label for tenecteplase (Metalyse) *available at*: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000306/WC500026892.pdf (HALOZ0001275-HALOZ0001331).

87. Attached as Exhibit 86 is a true and correct copy of the July 10, 2017 Rebuttal Report of Samuel Zalipsky, Ph.D.

88. Attached as Exhibit 87 is a true and correct copy of Gacesa *et al.*, *Functional Arginine Residues in Bovine Testicular Hyaluronidase,* BIOCHEM. SOCIETY TRANSACTIONS, 7(5):1058-1060 (1979) (HALOZ0008336-HALOZ0008338).

89. Attached as Exhibit 88 is a true and correct copy of Maksimenko *et al.*, *Aldehyde dextran modified enzymes for medical application*, Interbiotech '87: Enzyme Technologies, Blazej, A. and Zemek, J., Eds., Amsterdam: Elsevier, Progress in Biotechnology, 4:509-522 (1988) (HALOZ0008339-HALOZ0008354).

90. Attached as Exhibit 89 is a true and correct copy of Walter *et al.*, *Partitioning in Aqueous Two-Phase Systems: Recent Results*, ANALYT. BIOCHEM. 197:1-18 (1991) (HALOZ0008355-HALOZ0008372).

91. Attached as Exhibit 90 is a true and correct copy of Musu *et al.*, *Reversible*

Modification of Thiol-Containing Polypeptides with Poly(ethylene glycol) Through Formation of Mixed Disulfide Bonds – The Case of Papaya Proteinase III APPL. BIOCHEM. BIOTECHNOL. 56:243-263 (1996) (HALOZ0008373-HALOZ0008393).

92. Attached as Exhibit 91 is a true and correct copy of Paul *et al.*, *Preparation and Characterization of A S-Monomethoxypoly- (Ethylene Glycol) Thioderivative of Papain,* PHYTOCHEMISTRY 35:1413-1417 (1994) (HALOZ0008394-HALOZ0008398).

93. Attached as Exhibit 92 is a true and correct copy of Roberts and Harris, *Attachment of degradable poly(ethylene glycol) to proteins has the potential to increase therapeutic efficacy*, J. PHARM. SCI. 87:1440-1445 (1998) (HALOZ0008399-HALOZ0008404).

94. Attached as Exhibit 93 is a true and correct copy of Moriyama *et al.*, *Hyaluronic acid grafted with poly(ethylene glycol) as a novel peptide formation*, J. CONTROLLED REL. 59:77-86 (1999) (HALOZ0008405-HALOZ0008414).

95. Attached as Exhibit 94 is a true and correct copy of Maksimenko (Russian) (2000) (HALOZ0008415-HALOZ0008419).

96. Attached as Exhibit 95 is a true and correct copy of Vanwetswinkel *et al.*, *Pharmacokinetic and thrombolytic properties of cysteine-linked polyethylene glycol derivatives of staphylokinase*, BLOOD 95(3):936-942 (2000) (HALOZ0008420-HALOZ0008426).

97. Attached as Exhibit 96 is a true and correct copy of Lee *et al.*, *Drug delivery systems employing 1,6 elimination: Releasable poly(ethylene glycol) conjugates of proteins*, BIOCONJUGATE CHEM. 12:163-169 (2001) (HALOZ0008427-HALOZ0008433).

98. Attached as Exhibit 97 is a true and correct copy of Greenwald *et al.*, *Controlled Release of proteins from their poly(ethylene glycol) conjugates: Drug delivery systems employing 1,6-elimination*, BIOCONJUGATE CHEM. 14:395-403 (2003) (HALOZ0008434-

HALOZ0008442).

99. Attached as Exhibit 98 is a true and correct copy of Mei *et al.*, *Rational design of a fully active, long-acting PEGylated factor VIII for hemophilia A treatment*, BLOOD 116(2): 270-279 (2010) (HALOZ0008434-HALOZ0008442).

100. Attached as Exhibit 99 is a true and correct copy of Musu *et al.*, *Easy Purification of Ananain Through Reversible Pegylation* IJBC 1:17-27 (1994) (HALOZ0008453-HALOZ0008463).

101. Attached as Exhibit 100 is a true and correct copy of Xu *et al.*, *Polyethylene Glycol Modified FGF21 Engineered to Maximize Potency and Minimize Vacuole Formation*, BIOCONJUGATE CHEM. 24:915-925 (2013) (HALOZ0008464-HALOZ0008474).

102. Attached as Exhibit 101 is a true and correct copy of the July 10, 2017 Rebuttal Report of Bruno Flamion, Ph.D.

103. Attached as Exhibit 102 is a true and correct copy of Baumgartner *et al.*, *The impact of extracellular matrix on the chemoresistance of solid tumors – experimental and clinical results of hyaluronidase as additive to cytostatic chemotherapy*, CANCER LETTERS 131:85-99 (1998) (HALOZ0008475-HALOZ0008489).

104. Attached as Exhibit 103 is a true and correct copy of Hemming *et al.*, *Mouse Hyal3 encodes a 45- to 56-kDa glycoprotein whose overexpression increases hyaluronidase 1 activity in cultured cells*, GLYCOBIOLOGY 18(4):280-289 (2008) (HALOZ0008490-HALOZ0008499).

105. Attached as Exhibit 104 is a true and correct copy of Hofinger *et al.*, *Isoenzyme-specific differences in the degradation of hyaluronic acid by mammalian-type hyaluronidases*, GLYCOCONJ. J. 25:101-109 (2008) (HALOZ0008500-HALOZ0008508).

106. Attached as Exhibit 105 is a true and correct copy of Reitinger *et al.*, *High-yield recombinant expression of the extremophile enzyme, bee hyaluronidase in Pichia pastoris*, PROTEIN EXPRESSION & PURIFICATION 57:226-233 (2008) (HALOZ0008509-HALOZ0008516).

107. Attached as Exhibit 106 is a true and correct copy of Provenzano *et al.*, *Enzymatic Targeting of the Stroma Ablates Physical Barriers to Treatment of Pancreatic Ductal Adenocarcinoma*, CANCER CELL 21:418-429 (2012) (HALOZ0008517-HALOZ0008528).

108. Attached as Exhibit 107 is a true and correct copy of Defendants' Third Supplemental Responses to Halozyme's First Set of Interrogatories, dated July 14, 2017.

109. Attached as Exhibit 108 is a true and correct copy of excerpts from the July 26, 2017 deposition transcript of Bruno Flamion, Ph.D.

110. Attached as Exhibit 109 is a true and correct copy of excerpts from the July 21, 2017 deposition transcript of Zhaohui Zhou.

111. Attached as Exhibit 110 is a true and correct copy of excerpts from the July 19, 2017 deposition transcript of Samuel Zalipsky, Ph.D.

112. Attached as Exhibit 111 is a true and correct copy of excerpts from the June 23, 2017 Expert Report of Zhaohui Zhou.

113. Attached as Exhibit 112 is a true and correct certified copy of U.S. Patent Application No. 11/065,716 (the "'716 Application").

114. Attached as Exhibit 113 is a true and correct copy of excerpts from the June 30, 2017 deposition transcript of Dr. Gregory I. Frost.

115. Attached as Exhibit 114 is a true and correct copy of the July 10, 2017 Rebuttal Expert Report of Jon Saxe.

116. Attached as Exhibit 115 is a true and correct copy of the '171 Application

Assignment Record, recorded January 26, 2006 (PTO40000-PTO40005).

117. Attached as Exhibit 116 is a true and correct copy of the '171 Application Assignment Record, recorded March 17, 2009 (PTO40006-PTO40013).

118. Attached as Exhibit 117 is a true and correct copy of the '171 Application Assignment Record, recorded March 17, 2009 (PTO40014-PTO40021).

119. Attached as Exhibit 118 is a true and correct copy of the '171 Application Assignment Record, recorded March 17, 2009 (PTO40022-PTO40024).

120. Attached as Exhibit 119 is a true and correct copy of the '716 Application Assignment Record, recorded April 15, 2005 (PTO40025-PTO40030).

121. Attached as Exhibit 120 is a true and correct copy of the '716 Application Assignment Record, recorded March 17, 2009 (PTO40031-PTO40036).

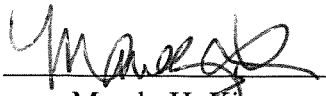
122. Attached as Exhibit 121 is a true and correct copy of the '716 Application Assignment Record, recorded March 17, 2009 (PTO40037-PTO40042).

123. Attached as Exhibit 122 is a true and correct copy of the '716 Application Assignment Record, recorded March 17, 2009 (PTO40043-PTO40045).

124. Attached as Exhibit 123 is a true and correct copy of excerpts from the June 20, 2017 deposition transcript of Michael LaBarre, Ph.D.

I declare under penalty of perjury of the laws of the United States of America, that the foregoing is true and correct. Executed this 8th day of September, 2017 in Irvine, California.

Dated: September 8, 2017

By: 
Mandy H. Kim